REMARKS

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the amendments and remarks herewith, which place the application into condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-18, 23, 24 and 26-75 are under consideration in this application. Claims 1, 3, 4, 6-9, 11-18, 23, 24 and 26-29 have been amended. Claims 2, 5 and 10 have been cancelled. Claims 30-75 have been added.

Support for the amended and added claims can be found throughout the specification. Specifically, claim 1 has been amended to include the limitations of cancelled claims 2, 5 and 10. Support for the amendment to claim 13 can be found on page 11, lines 6-9 of the application and from claim 13 as originally filed. Dependent claims 30 and 31 include subject matter originally recited in claim 13. Dependent claims 32-36 include subject matter originally recited in claims 23 and 26. Dependent claim 37 recites subject matter that was removed from claim 3. Dependent claims 38 and 39 contain subject matter originally included in claim 11.

Support for claim 40 can be found on page 6, lines 3-7 and 11-13 and on page 9, lines 2-6 of the application. Details of the coupling system, including the subject matter recited in claims 41 and 42, can be found in the paragraph of the specification bridging pages 6 and 7. Support for claim 44 can be found in Example 1.

Claims 46-75 mirror the other pending claims, and contain language that more specifically defines the coupling system.

Support for the remaining amendments can be found throughout the specification. Several amendments were made to correct informalities and to place the claims in better form. No new matter is added by these amendments.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. §112. The amendments of and additions to the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel, as the herewith amendments are not narrowing amendments.

Priority

The Examiner is thanked for acknowledging the claim for foreign priority. Certified copies of foreign priority documents UK application no. 9812227.8 and UK application no. 9908333.9 were filed via Express Mail on December 31, 2003. It is believed that the requirements under 35 U.S.C. §119(b) have been fulfilled.

Drawings

New corrected drawings in response to the Drawing Review are attached. Reconsideration and withdrawal of the objections to the drawings are requested.

Specification

A new, executed declaration is attached, as required by the Office Action. Reconsideration and withdrawal of the objection to the specification are requested.

Claims

Claims 1, 12 and 16 were objected to for various informalities. These claims have been amended to overcome the objections. Reconsideration and withdrawal of the objections to the claims are requested.

II. THE REJECTIONS UNDER 35 U.S.C. §112, 2nd PARAGRAPH, ARE OVERCOME

Claims 13, 23, 24 and 26-29 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Claim 13 has been amended to remove the recitation "such as" and the combination of a broad limitation and a narrower limitation in the same claim. Dependent claims 30 and 31 have been added to cover the subject matter previously included in claim 13. Reference to claims 10 and 12 has also been removed from claim 13.

Claims 23 and 26 have been amended to remove the recitation "such as" from each claim. Claims 32-36 have been added to cover the subject matter previously included in claims 23 and 26.

The recitation "said compound" has been removed from claim 29.

Claim 27 has been amended such that is now recites method steps. Although claim 24 was not included in this rejection, it has been so amended as well.

The claims are believed to be in compliance with the requirements of 35 U.S.C. §112, second paragraph. Reconsideration and withdrawal of the rejections under §112, second paragraph, are requested.

III. THE REJECTION UNDER 35 U.S.C. §112, 1st PARAGRAPH, IS OVERCOME

Claims 23, 24 and 26-29 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The rejection is traversed.

The Office Action alleges that "[t]he instant specification provides only in vitro exemplifications of the recited complexes", and further goes on to state that "[t]he in vivo uses of the recited complexes is unpredictable".

MPEP 2164.02(c) provides guidelines to follow in determining whether a showing of success by an applicant using *in vitro* data supports claims directed to the analogous *in vivo* application. An *in vitro* model is acceptable where it is recognized in the art that this model correlates to a specific *in vivo* condition. If this is has not yet been established in the art, the *in vitro* model is acceptable if one skilled in the art would accept the model as *reasonably* correlating to the condition. The "reasonableness" standard serves to prevent the PTO from unnecessarily and inappropriately adopting the more stringent standards of the FDA.[1]

In the present invention, the "condition" of MPEP 2164.02(c) is the presence of diseased, foreign or malignant cells in a patient. The "condition" can be alleviated by specifically targeting the diseased, foreign or malignant cells for destruction by the patient's immune system. When testing a therapy for immunological targeting of unwanted cells, a good experimental model should test whether 1) the therapy will target the cells of interest and whether 2) the target cells are eliminated as a result. If this test is carried out *in vitro* and it is successful, the result is reasonably predictive of success *in vivo.*

For the inventive methods, results *in vitro* have been shown to correlate with results *in vivo*. The teaching in Example 1 of the specification demonstrates that the complexes of the invention (exemplified by an HLA-A2/gag complex), attach to the surface of human melanoma cells (Mel 1). Upon incubation with HLA-A2/gag specific cytotoxic T cells, the melanoma cells

[1] Public hearings were held in San Diego on October 17, 1994, where then PTO Commissioner Bruce Lehman and other PTO representatives received comments on the inappropriate standards that Examiners were applying to biotechnological inventions and as a result of these and other objections raised by the scientific community, the present "reasonableness" standard is now applied.

are lysed. Targeted lysis of Daudi cells and SK-mel-29 and MM9 melanoma cells in a similar manner is demonstrated in Example 2.

The Applicants should not be required to provide further experimental data in order for the full scope of the claims to be allowed. Given the strong showing of success with the inventive methods *in vitro*, the full scope of the claims is allowable. A rigorous or an invariable exact correlation between *in vitro* and *in vivo* results is not required, as stated in *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747 (Fed. Cir. 1985) ("based upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed in vitro utility and an in vivo activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence); *see also In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436 1441 (Fed. Cir. 1995) (reversing the PTO decision based on finding that *in vitro* data did not support *in vivo* applications). Further experimentation, such as in human subjects, is clearly not required. The PTO is not the FDA.

Accordingly, the full scope of the claims is enabled, and reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are requested.

IV. THE REJECTION UNDER 35 U.S.C. §102 IS OVERCOME

Claims 1-7, 9-12 and 14-18 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Mage *et al.* The rejection is traversed.

There are several differences between the ideas discussed in Mage and the instant invention. For instance, Mage requires the use of polyacrylamide in the coupling system, which that is not contemplated by the current invention. Mage also suggests the use of HLA allogenic molecules, while the instant invention is focussed on autologous HLA molecules. Finally, the Mage approach would produce large molecules that would be unlikely to localize properly to a tumor.

Although it is believed that the instant invention is not anticipated by Mage, claims 46-75 have been added with "consists essentially of" language with respect to the coupling system. This should make it clear that polyacrylamide is excluded from the invention and that the claims, therefore, are novel over Mage.

It is noted that the transition "consists essentially of" occupies a middle ground between "comprises" and "consists of". It allows for elements not explicitly recited, but excludes elements that are found in the prior art or that affect a basic or novel characteristic of the invention. *See,*

e.g., In re Garnero, 162 U.S.P.Q. 221 (C.C.P.A. 1969); *Ex parte Shepherd*, 185 U.S.P.Q. 480 (BOPA 1974); *Ex parte Hutchins,* 157 U.S.P.Q. 167 (BOPA 1967); *see also Zeigler v. Phillips Petroleum Co.*, 177 U.S.P.Q. 481 (5th Cir. 1973). Thus, the claims, by their terms, distinguish from the document cited.

Consequently, reconsideration and withdrawal of the rejection under 35 U.S.C. §102 are requested.

CONCLUSION

In view of the amendments and remarks herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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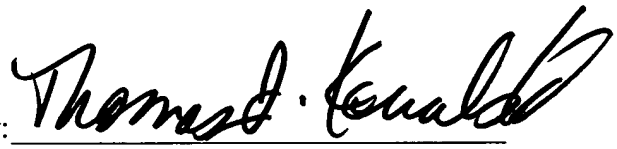
By: 

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